

Application No.: 10/740,264

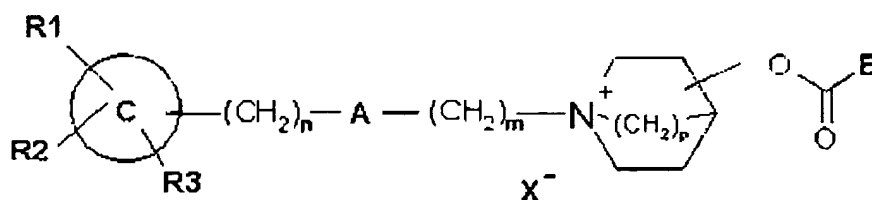
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AMENDMENTS TO THE CLAIMS

Claims 1-35 (cancelled)

Claim 36 (previously presented): A compound according to formula (I)



(I)

wherein:

© is a phenyl ring, a C<sub>4</sub> to C<sub>9</sub> heteroaromatic group containing one or more heteroatoms or a naphthalenyl, 5,6,7,8-tetrahydronaphthalenyl or biphenyl group;

R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> each independently represent a hydrogen atom or halogen atom, or a hydroxy group, or a phenyl, -OR<sup>4</sup>, -SR<sup>4</sup>, -NR<sup>4</sup>R<sup>5</sup>, -NHCOR<sup>4</sup>, -CONR<sup>4</sup>R<sup>5</sup>, -CN, -NO<sub>2</sub>, -COOR<sup>4</sup> or -CF<sub>3</sub> group, or a straight or branched lower alkyl group which may optionally be substituted with a hydroxy or alkoxy group, wherein R<sup>4</sup> and R<sup>5</sup> each independently represent a hydrogen atom, straight or branched lower alkyl group or together form an alicyclic ring; or R<sup>1</sup> and R<sup>2</sup> together form an aromatic, alicyclic or heterocyclic ring,

n is an integer from 0 to 4;

A represents a -CH<sub>2</sub>-, -CH=CR<sup>6</sup>-, -CR<sup>6</sup>=CH-, -CR<sup>6</sup>R<sup>7</sup>-, -CO-, -O-, -S-, -S(O)-, SO<sub>2</sub> or -NR<sup>6</sup>- group, wherein R<sup>6</sup> and R<sup>7</sup> each independently represent a hydrogen atom, straight or branched lower alkyl group or R<sup>6</sup> and R<sup>7</sup> together form an alicyclic ring;

m is an integer from 0 to 8; provided that when m = 0, A is not -CH<sub>2</sub>-;

p is an integer from 1 to 2 and the substitution in the azoniabicyclic ring may be in the 2, 3 or 4 position including all possible configurations of the asymmetric carbons;

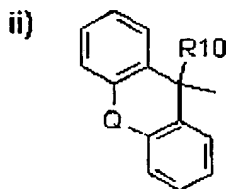
B represents a group of formula ii):

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wherein  $R^{10}$  represents a hydrogen atom, a hydroxy or methyl group;  
and Q represents a single bond,  $-CH_2-$ ,  $-CH_2-CH_2-$ ,  $-O-$ ,  $-O-CH_2-$ ,  $-S-$ ,  $-S-CH_2-$  or  $-CH=CH-$ ; and  
X represents a pharmaceutically acceptable anion of a mono or polyvalent acid.

Claim 37 (previously presented): A compound according to claim 36, wherein any alkyl group present as  $R^1$  to  $R^7$  contains from 1 to 4 carbon atoms.

Claim 38 (previously presented): A compound according to claim 36 wherein  $p=2$ .

Claim 39 (previously presented): A compound according to claim 36 wherein © represents a phenyl, pyrrolyl, thienyl, furyl, biphenyl, naphthalenyl, 5,6,7,8-tetrahydronaphthalenyl, benzo[1,3]dioxolyl, imidazolyl or benzothiazolyl group.

Claim 40 (previously presented): A compound according to claim 39, wherein © represents a phenyl, pyrrolyl or thienyl group.

Claim 41 (previously presented): A compound according to claim 36 wherein  $R^1$ ,  $R^2$  and  $R^3$  each independently represent a hydrogen or halogen atom or a hydroxy, methyl, tert-butyl,  $-CH_2OH$ , 3-hydroxypropyl,  $-OMe$ ,  $-NMe_2$ ,  $-NHCOMe$ ,  $-CONH_2$ ,  $-CN$ ,  $-NO_2$ ,  $-COOMe$  or  $-CF_3$  group.

Claim 42 (previously presented): A compound according to claim 41 wherein  $R^1$ ,  $R^2$  and  $R^3$  each independently represent a hydrogen or halogen atom or a hydroxy group.

Claim 43 (previously presented): A compound according to claim 42, wherein the halogen atom is fluorine.

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Claim 44 (previously presented): A compound according claim 36 wherein A represents a  $-\text{CH}_2-$ ,  $-\text{CH}=\text{CH}-$ ,  $-\text{CO}-$ ,  $-\text{NH}-$ ,  $-\text{NMe}-$ ,  $-\text{O}-$  or  $-\text{S}-$  group; n is 0 or 1; and m is an integer from 1 to 6.

Claim 45 (previously presented): A compound according to claim 44, wherein A represents a  $-\text{CH}_2-$ ,  $-\text{CH}=\text{CH}-$  or  $-\text{O}-$  group and m is 1, 2 or 3.

Claim 46 (previously presented): A compound according claim 36 wherein the azoniabicyclo group is substituted on the nitrogen atom with a 3-phenoxypropyl, 2-phenoxyethyl, 3-phenylallyl, phenethyl, 3-phenylpropyl, 4-phenylbutyl, 3-(2-hydroxyphenoxy)propyl, 3-(4-fluorophenoxy)propyl, 2-benzyloxyethyl, 3-pyrrol-1-ylpropyl, 2-thien-2-ylethyl or 3-thien-2-ylpropyl group.

Claim 47 (previously presented): A compound according claim 36, wherein Q represents a single bond, a  $-\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2-$  group or an oxygen atom.

Claim 48 (previously presented): A compound according claim 36 wherein X represents a bromide, chloride or trifluoroacetate anion.

Claim 49 (previously presented): A compound according to claim 36 wherein the azoniabicyclo group is substituted in the 3-position.

Claim 50 (previously presented): A compound according to claim 49, wherein the substituent in the 3 position has (R) configuration.

Claim 51 (previously presented): A compound according to claim 36 which is a single stereoisomer.

Claim 52 (previously presented): A compound according to claim 36 which is 1-(3-phenylallyl)-3(R)-(9-Hydroxy-9[H]-fluorene-9-carbonyloxy)-1-azoniabicyclo[2.2.2]octane; bromide

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3(R)-(9-Hydroxy-9[H]-fluorene-9-carbonyloxy)-1-(3-phenoxypropyl)-1-azoniabicyclo  
[2.2.2]octane; bromide

3(R)-(9-Hydroxy-9[H]-fluorene-9-carbonyloxy)-1-phenethyl-1-  
azoniabicyclo[2.2.2]octane; bromide

3(R)-(9-Hydroxy-9H-fluorene-9-carbonyloxy)-1-(3-thien-2-ylpropyl)-1-azoniabicyclo  
[2.2.2]octane; bromide

3(R)-(9-Methyl-9[H]-fluorene-9-carbonyloxy)-1-(3-phenylallyl)-1-  
azoniabicyclo[2.2.2]octane; bromide

3(R)-(9-Methyl-9[H]-fluorene-9-carbonyloxy)-1-(3-phenoxypropyl)-1-azoniabicyclo  
[2.2.2]octane; bromide

1-(4-Phenylbutyl)-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-  
azoniabicyclo[2.2.2]octane; bromide

1-(2-Phenoxyethyl)-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-  
azoniabicyclo[2.2.2]octane; bromide

1-(3-Phenoxypropyl)-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-  
azoniabicyclo[2.2.2]octane; bromide

1-Phenethyl-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-azoniabicyclo  
[2.2.2] octane; bromide

3(R)-(9-Hydroxy-9[H]-xanthene-9-carbonyloxy)-1-(3-phenoxypropyl)-1- azoniabicyclo  
[2.2.2]octane; bromide

3(R)-(9-Hydroxy-9[H]-xanthene-9-carbonyloxy)-1-phenethyl-1-  
azoniabicyclo[2.2.2]octane; bromide

3(R)-(9-Hydroxy-9H-xanthene-9-carbonyloxy)-1-(3-thien-2-ylpropyl)-1-azoniabicyclo  
[2.2.2]octane; bromide or

3(R)-(9-Methyl-9[H]-xanthene-9-carbonyloxy)-1-(3-phenoxy-propyl)-1-azoniabicyclo  
[2.2.2]octane; bromide.

Claim 53 (previously presented): A compound according to claim 36, wherein it has an IC<sub>50</sub>  
value for muscarinic M<sub>3</sub> receptors (Hm3) of less than 35 nM.

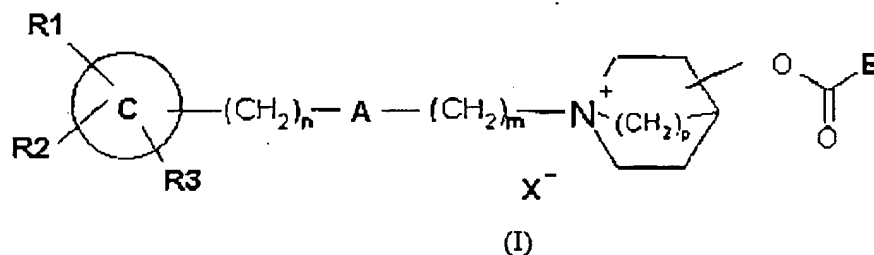
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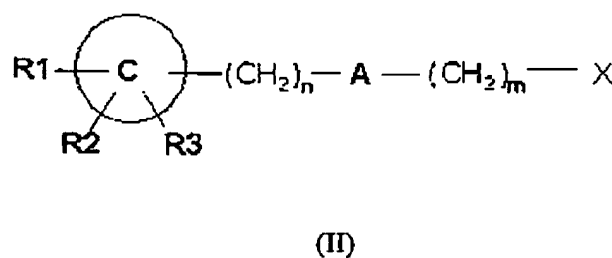
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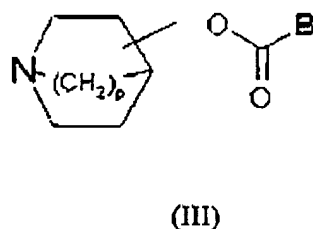
Claim 54 (previously presented): A process for the preparation of a compound of formula (I)



which comprises reacting an alkylating agent of formula (II)



with a compound of formula (III)



to obtain a reaction mixture comprising the compound of formula (I), wherein, in each of formulae I, II and III, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, C, A, X, B, n, m and p are as defined in claim 36.

Claim 55 (previously presented): A process according to claim 54, wherein the reaction mixture is purified by solid phase extraction.

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Claim 56- 60 (cancelled)

Claim 61 (previously presented): A pharmaceutical composition comprising a compound according to claim 36 in admixture with a pharmaceutically acceptable carrier or diluent.

Claim 62 (cancelled).

Claim 63 (currently amended): A method for treating COPD, chronic bronchitis, bronchial hyperreactivity, asthma and/or rhinitis which method comprises administering to a human or animal patient in need of such treatment an effective amount of a compound according to any one of claims 36-53 or of a pharmaceutical composition according to claim 61.

Claim 64 (new): A pharmaceutical composition according to claim 61, wherein the pharmaceutically acceptable carrier or diluent is aqueous.

Claim 65 (new): A compound according to claim 36, wherein the compound is 1-Phenethyl-3(R)-(9[H]-xanthene-9-carboxyloxy)-1-azoniabicyclo [2.2.2] octane; X-, wherein X- is a pharmaceutically acceptable anion of a mono or polyvalent acid.

Claim 66 (new): A compound according to claim 65, wherein X- is Br-.

Claim 67 (new): A pharmaceutical composition according to claim 61 or 64, wherein the compound is 1-Phenethyl-3(R)-(9[H]-xanthene-9-carboxyloxy)-1-azoniabicyclo [2.2.2] octane; X-, wherein X- is a pharmaceutically acceptable anion of a mono or polyvalent acid.

Claim 68 (new): A pharmaceutical composition according to claim 67 wherein X- is Br-.

Claim 69 (new): A method for treating COPD, chronic bronchitis, bronchial hyperreactivity, asthma and/or rhinitis which method comprises administering to a human or animal

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patient in need of such treatment an effective amount of 1-Phenethyl-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-azoniabicyclo [2.2.2] octane; X<sup>-</sup>; or

administering to a human or animal patient in need of such treatment an effective amount of a pharmaceutical composition comprising 1-Phenethyl-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-azoniabicyclo [2.2.2] octane; X<sup>-</sup>, and wherein:

X<sup>-</sup> is a pharmaceutically acceptable anion of a mono or polyvalent acid.

Claim 70 (new): A method according to claim 69, wherein X<sup>-</sup> is Br<sup>-</sup>.

Claim 71 (new): A pharmaceutical composition prepared by mixing a compound according to claim 36 with a pharmaceutically acceptable carrier or diluent.

Claim 72 (new): A pharmaceutical composition according to claim 71, wherein the pharmaceutically acceptable carrier or diluent is aqueous.

Claim 73 (new): A pharmaceutical composition according to claim 71 or 72, wherein the compound is 1-Phenethyl-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-azoniabicyclo [2.2.2] octane; X<sup>-</sup>, and wherein:

X<sup>-</sup> is a pharmaceutically acceptable anion of a mono or polyvalent acid.

Claim 74 (new): A pharmaceutical composition according to claim 73, wherein X<sup>-</sup> is Br<sup>-</sup>.

Claim 75 (new): A method for treating COPD, chronic bronchitis, bronchial hyperreactivity, asthma and/or rhinitis, which method comprises administering to a human or animal patient in need of such treatment an effective amount of a pharmaceutical composition according to claim 71.

Claim 76 (new): A method according to claim 75, wherein the pharmaceutically acceptable carrier or diluent is aqueous.

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Claim 77 (new): A method according to claim 75 or 76, wherein the compound is 1-Phenethyl-3(R)-(9[H]-xanthene-9-carboxyloxy)-1-azoniabicyclo [2.2.2] octane; X-, and wherein: X- is a pharmaceutically acceptable anion of a mono or polyvalent acid.

Claim 78 (new): A method according to claim 77, wherein X- is Br-.

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